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1-Year Outcomes After Transcatheter Aortic Valve Replacement With Balloon-Expandable Versus Self-Expandable Valves

Results From the CHOICE Randomized Clinical Trial

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ABSTRACT

BACKGROUND The use of a balloon-expandable transcatheter heart valve previously resulted in a greater rate of device success compared with a self-expandable transcatheter heart valve.

OBJECTIVES The aim of this study was to evaluate clinical and echocardiographic outcome data at longer term follow-up.

METHODS The investigator-initiated trial randomized 241 high-risk patients with symptomatic severe aortic stenosis and anatomy suitable for treatment with both balloon- and self-expandable transcatheter heart valves to transfemoral transcatheter aortic valve replacement with either device. Patients were followed-up for 1 year, with assessment of clinical outcomes and echocardiographic evaluation of valve function.

RESULTS At 1 year, the rates of death of any cause (17.4% vs. 12.8%; relative risk [RR]: 1.35; 95% confidence interval [CI]: 0.73 to 2.50; p = 0.37) and of cardiovascular causes (12.4% vs. 9.4%; RR: 1.32; 95% CI: 0.63 to 2.75; p = 0.54) were not statistically significantly different in the balloon- and self-expandable groups, respectively. The frequencies of all strokes (9.1% vs. 3.4%; RR: 2.66; 95% CI: 0.87 to 8.12; p = 0.11) and repeat hospitalization for heart failure (7.4% vs. 12.8%; RR: 0.58; 95% CI: 0.26 to 1.27; p = 0.19) did not statistically significantly differ between the 2 groups. Elevated transvalvular gradients during follow-up were observed in 4 patients in the balloon-expandable group (3.4% vs. 0%; p = 0.12); all were resolved with anticoagulant therapy, suggesting a thrombotic etiology. More than mild paravalvular regurgitation was more frequent in the self-expandable group (1.1% vs. 12.1%; p = 0.005).

CONCLUSIONS Despite the higher device success rate with the balloon-expandable valve, 1-year follow-up of patients in CHOICE (Randomized Comparison of Transcatheter Heart Valves in High Risk Patients With Severe Aortic Stenosis: Medtronic CoreValve Versus Edwards SAPIEN XT Trial), with limited statistical power, revealed clinical outcomes after transfemoral transcatheter aortic valve replacement with both balloon- and self-expandable prostheses that were not statistically significantly different. (A Comparison of Transcatheter Heart Valves in High Risk Patients With Severe Aortic Stenosis: The CHOICE Trial; NCT01645202) (J Am Coll Cardiol 2015;66:791–800) © 2015 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

AR = aortic regurgitation

CI = confidence interval

NYHA = New York Heart Association

RR = relative risk

TAVR = transcatheter aortic valve replacement

THV = transcatheter heart valve

VARC = Valve Academic Research Consortium

In the past decade, transcatheter aortic valve replacement (TAVR) has evolved from a novel technology to an established therapy for high-risk patients with severe symptomatic aortic valve stenosis (1–3). Currently, several transcatheter heart valves (THVs) have been approved or are being evaluated in clinical trials, but broadly, there are 2 main THVs in clinical use: balloon-expandable and self-expandable valves. Numerous studies have been published on the safety and efficacy of both device types separately, and both technologies have been associated with favorable short- and long-term outcomes (1–7). However, comparative data are scarce and have been derived mainly from observational registries (8–11).

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In CHOICE (Randomized Comparison of Transcatheter Heart Valves in High Risk Patients With Severe Aortic Stenosis: Medtronic CoreValve Versus Edwards SAPIEN XT), the first head-to-head trial of balloon- and self-expandable THVs, the use of a balloon-expandable valve resulted in a greater rate of device success than the use of a self-expandable valve, while clinical outcomes at 30 days were comparable (12). In this report, we describe the 1-year clinical outcomes and echocardiographic findings after TAVR with balloon- and self-expandable valves in the CHOICE trial.

METHODS

STUDY DESIGN AND POPULATION. The study design and patient selection of the CHOICE trial have been previously described (12). Briefly, this investigator-initiated, multicenter, randomized controlled trial included 241 patients with symptomatic severe aortic stenosis at high risk for surgical aortic valve replacement undergoing TAVR through the transfemoral route at 5 German centers. Patients had to be anatomically suitable for treatment with both balloon- and self-expandable valves, which was defined as a native aortic valve annulus measuring 20 to 27 mm in diameter on pre-procedural imaging. Patients with pre-existing aortic bioprostheses and/or contraindications to transfemoral access were excluded. The study was in compliance with the Declaration of Helsinki, the locally appointed ethics committees approved the research protocol, and written informed consent was obtained from all subjects. An independent data-coordinating center, with oversight from a steering committee, conducted the data management and analysis. The members of the steering committee had full access to the data and vouch for the accuracy and completeness of the data and the analyses.

STUDY DEVICES AND PROCEDURE. The devices used in this study and the TAVR procedure have been previously described (12–14). The balloon-expandable valve used in this trial (Edwards SAPIEN XT; Edwards Lifesciences, Irvine, California) is a cylindrical cobalt-chromium stent into which 3 leaflets made of bovine pericardium are mounted, whereas the self-expandable valve (Medtronic CoreValve; Medtronic Inc., Minneapolis, Minnesota) consists of porcine pericardial tissue sewn to form a trileaflet valve mounted within a self-expanding hourglass-shaped nitinol frame. Device size selection was based largely on 3-dimensional multidetector computed tomography-based annular measurements. Highly experienced operators at centers with established multidisciplinary TAVR programs performed all procedures, and these were mainly accomplished under analgo-sedation (without endotracheal intubation) using fluoroscopic guidance. Antithrombotic treatment recommendation consisted of aspirin 100 mg/day indefinitely and clopidogrel 75 mg for at least 3 months. Patients taking oral anticoagulant agents mainly continued oral anticoagulation and were prescribed clopidogrel for 3 months but no aspirin.

STUDY ENDPOINTS. The pre-specified primary endpoint of the CHOICE trial was "device success," as defined by the first Valve Academic Research Consortium (VARC) consensus document (15) and has been previously reported (12). All patients were followed-up for at least 1 year and had clinical visits and echocardiographic evaluations at 6 months and 1 year. Pre-specified secondary endpoints included cardiovascular mortality, stroke, repeat hospitalization for heart failure, New York Heart Association (NYHA) functional class improvement (improvement

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by at least 1 functional class), a combined efficacy endpoint (a composite of all-cause mortality between 30 days and 1 year, failure of current therapy for aortic stenosis requiring hospitalization for symptoms of valve-related or cardiac decompensation, and prosthetic valve dysfunction, defined as an aortic valve area <1.2 cm^2 and mean aortic valve gradient >20 mm Hg or peak velocity >3 m/s or moderate or severe prosthetic valve regurgitation), and major adverse cardiovascular and cerebrovascular events (a composite of myocardial infarction, cardiac or vascular surgery, and stroke). A clinical events committee blinded to treatment assignment was responsible for adjudicating all endpoints. Definitions of the endpoints were identical to those in the original trial (in accordance with the first VARC consensus document) and have been reported elsewhere (12,15).

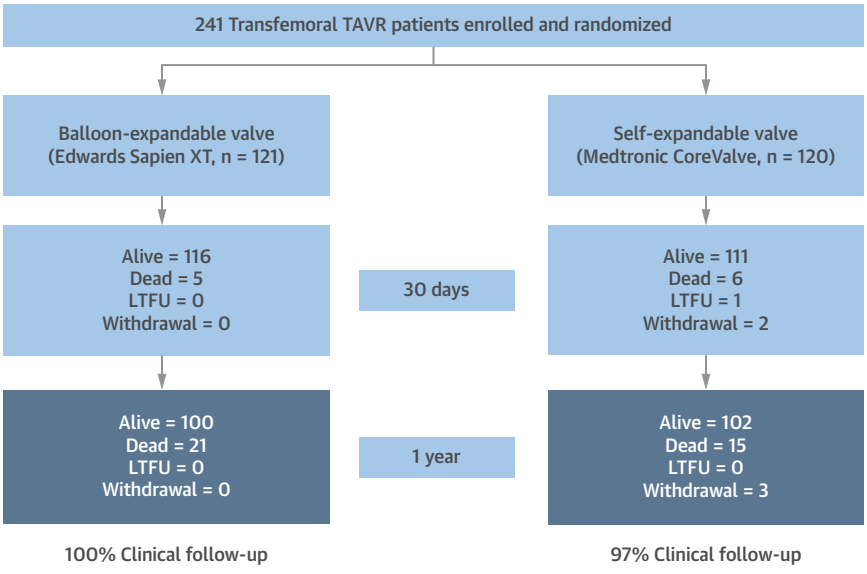
Echocardiographic assessment was performed in accordance with the VARC recommendations (15). Aortic regurgitation (AR) was semiquantitatively assessed by estimating the proportion of the circumference of the valved stent occupied by the jet: <10% was graded as mild, 10% to 20% as moderate, and >20% as severe paravalvular AR (15,16). Evaluation was performed on site by an experienced interventional echocardiographer blinded to the echocardiographic findings at discharge and/or 30 days.

STATISTICAL ANALYSIS. The sample size of the trial was based on the original primary endpoint of device success, as previously described (12). With the sample size of 241 patients and an annual mortality rate of 15%, the trial had approximately 50% power to detect a 10% difference in 1-year mortality between both treatment arms, with a 5% significance level. All clinical and echocardiographic endpoints were analyzed on an intention-to-treat basis. Categorical variables were compared using the Fisher exact test, and the relative risk (RR) and 95% confidence interval (CI) were calculated using a standard method (17). Continuous variables were compared using 2-sided unpaired Student *t* test or Mann-Whitney *U* tests, as appropriate. Survival curves for time-to-event variables were constructed using Kaplan-Meier estimates on the basis of all available data and were compared using log-rank tests. Death was treated as a censoring event in the Kaplan-Meier analysis for all strokes and rehospitalization for heart failure. All tests were 2-sided, and p values <0.05 were considered to indicate statistical significance. Statistical analyses were performed using Minitab version 15 (Minitab Inc., State College, Pennsylvania) and SAS version 9.4 (SAS Institute Inc., Cary, North Carolina). An independent statistician performed all analyses.

RESULTS

PATIENTS. Two hundred forty-one patients undergoing transfemoral TAVR were enrolled between March 2012 and December 2013; 121 patients were

FIGURE 1 Study Flowchart



LTFU = lost to follow-up; TAVR = transcatheter aortic valve replacement.

randomized to the balloon-expandable valve and 120 patients to the self-expandable valve. All patients received the assigned TAVR device, with no crossovers. Figure 1 shows the study-group assignments and follow-up. All patients were followed-up for 1 year. The overall study population was elderly (mean age 81.5 ± 6.2 years), had severe cardiac symptoms (80.9% were in NYHA functional class III or IV), and had frequent comorbid conditions (63.1% had histories of coronary artery disease, 39.4% had undergone previous percutaneous coronary intervention, 14.1% had undergone previous coronary artery bypass surgery, 17.4% had peripheral vascular disease, and 21.2% had pulmonary disease). The balloon- and self-expandable groups were generally well balanced with regard to baseline clinical and echocardiographic characteristics (Table 1), except for sex (43.0% men in the balloon-expandable group and 28.3% in the self-expandable group, p = 0.02). The mean logistic European System for Cardiac Operative Risk Evaluation score was 21.8 ± 13.8%, and the mean Society of Thoracic Surgeons score was 5.9 ± 3.5%.

CLINICAL OUTCOMES. Outcomes at 30 days have been previously described (12). Between 30 days and 1 year, there were 16 additional deaths in the balloon-expandable group and 9 in the self-expandable group. At 1 year, there was no significant evidence of a difference in mortality of any cause between the balloon-expandable group (17.4%) and the self-expandable group (12.8%; RR: 1.35; 95% CI: 0.73 to 2.50; p = 0.37) (Table 2, Figure 2). Cardiovascular mortality at 1 year was not statistically significantly different between the balloon- and self-expandable groups (12.4% and 9.4%, respectively; RR: 1.32; 95% CI: 0.63 to 2.75; p = 0.54). Eight patients (4 from each group) had sudden or unexplained death during the follow-up period.

Between 30 days and 1 year, 5 strokes occurred (4 in the balloon-expandable group and 1 in the self-expandable group). The frequency of all strokes at 1 year was numerically but not statistically significantly higher with the balloon-expandable valve compared with the self-expandable valve (9.1% vs. 3.4%; RR: 2.66; 95% CI: 0.87 to 8.12; p = 0.11) (Table 2, Figure 3). The composite of the rate of death of any cause or stroke did not statistically significantly differ between the 2 treatment groups (21.5% vs. 15.4%; RR: 1.40; 95% CI: 0.81 to 2.41; p = 0.25).

Other clinical events are summarized in Table 2. Vascular and bleeding complications were observed mainly during the periprocedural period, but after 30 days, these events were uncommon and did not statistically significantly differ between the 2 treatment groups. Endocarditis, as defined by the modified Duke criteria, was rare and was not statistically significantly different between both groups (2 cases of definite endocarditis in the balloon-expandable group and 1 case of possible endocarditis in the self-expandable group). Between 30 days and 1 year, 7 patients required new pacemakers, all from the balloon-expandable group. Nevertheless, the cumulative rate of new pacemaker implantation at 1 year remained higher in the self-expandable group (23.4% vs. 38.0%; p = 0.02). Overall, 49% of pacemaker implantations were performed for indications other than advanced atrioventricular block, with no statistically significant difference between the balloon- and self-expandable groups (46.2% vs. 51.4%; p = 0.80).

At 1 year, there was no statistically significant difference in the rate of repeat hospitalization for heart failure between the groups (7.4% in the balloon-expandable group vs. 12.8% in the self-expandable group; RR: 0.58; 95% CI: 0.26 to 1.27; p = 0.19) (Table 2, Figure 3). Of the 24 patients requiring rehospitalization for heart failure during the follow-up period, 6 had more than mild residual AR after TAVR, all in the self-expandable group (40% of heart failure hospitalizations in this group). Among survivors at 1

TABLE 1 Baseline Clinical Characteristics and Echocardiographic Findings

	Balloon-Expandable Valve (n = 121)	Self-Expandable Valve (n = 120)	p Value
Age, yrs	81.9 ± 6.7	79.6 ± 15.8	0.14
Women	69/121 (57.0)	86/120 (71.7)	0.02
Logistic EuroSCORE	21.5 ± 12.9	22.1 ± 14.7	0.72
Society of Thoracic Surgeons score	5.6 ± 2.9	6.2 ± 3.9	0.17
New York Heart Association functional class			0.79
I	7/121 (5.8)	4/120 (3.3)	
II	17/121 (14.1)	18/120 (15.0)	
III	73/121 (60.3)	74/120 (61.7)	
IV	24/121 (19.8)	24/120 (20.0)	
Coronary artery disease	73/121 (60.3)	79/120 (65.8)	0.38
Previous myocardial infarction	14/121 (11.6)	16/120 (13.3)	0.68
Previous CABG	19/121 (15.7)	15/120 (12.5)	0.48
Previous PCI	44/121 (36.4)	51/120 (42.5)	0.33
Cerebral vascular disease	26/121 (21.5)	22/120 (18.3)	0.54
Peripheral vascular disease	20/121 (16.5)	22/120 (18.3)	0.88
Pulmonary disease	27/121 (22.3)	24/120 (20.0)	0.66
Creatinine level, mg/dl	1.1 ± 0.4	1.2 ± 0.5	0.18
Atrial fibrillation	39/117 (33.3)	29/117 (24.8)	0.15
Permanent pacemaker	7/117 (5.9)	9/117 (7.7)	0.60
Echocardiography			
Aortic valve area, cm^2	0.7 ± 0.2	0.7 ± 0.2	0.71
Mean gradient, mm Hg	43.3 ± 15.4	43.0 ± 13.9	0.90
LV ejection fraction, %	52.5 ± 13.8	54.9 ± 11.9	0.15

Values are mean ± SD or n/N (%).

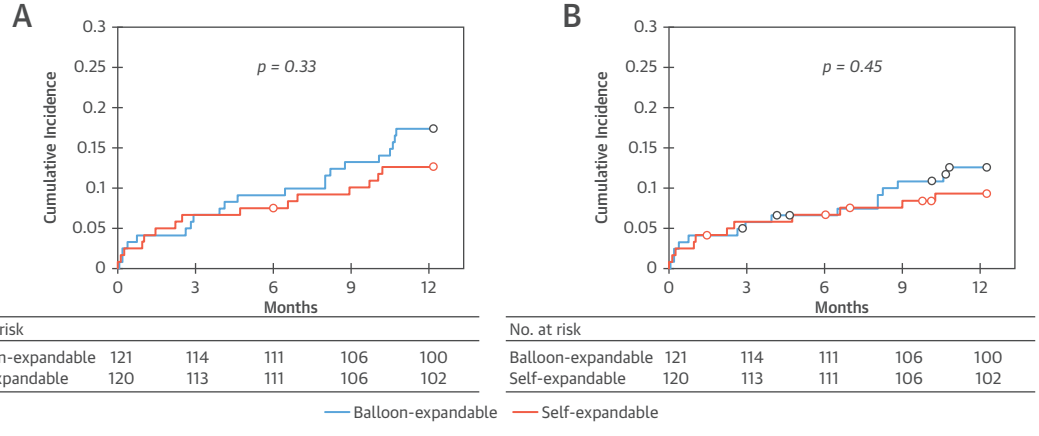
CABG = coronary artery bypass grafting; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LV = left ventricular; PCI = percutaneous coronary intervention.

TABLE 2 Clinical Outcomes at 1 Year

	Balloon-Expandable Valve (n = 121)	Self-Expandable Valve (n = 117)	RR (95% CI)	p Value
Death				
Of any cause	21/121 (17.4)	15/117 (12.8)	1.35 (0.73–2.50)	0.37
Of cardiovascular causes	15/121 (12.4)	11/117 (9.4)	1.32 (0.63–2.75)	0.54
Stroke	11/121 (9.1)	4/117 (3.4)	2.66 (0.87–8.12)	0.11
Major stroke	7/121 (5.8)	4/117 (3.4)	1.69 (0.51–5.63)	0.54
Minor stroke	4/121 (3.3)	0/117 (0.0)	–	0.12
Ischemic stroke	8/121 (6.6)	4/117 (3.4)	1.93 (0.60–6.25)	0.38
Hemorrhagic stroke	3/121 (2.5)	0/117 (0.0)	–	0.25
Repeat hospitalization for heart failure	9/121 (7.4)	15/117 (12.8)	0.58 (0.26–1.27)	0.19
Myocardial infarction	1/121 (0.8)	1/117 (0.9)	0.97 (0.06–15.28)	1.00
Bleeding				
Life threatening	17/121 (14.0)	15/117 (12.8)	1.10 (0.57–2.09)	0.85
Major	26/121 (21.5)	17/117 (14.5)	1.48 (0.85–2.58)	0.18
Minor	13/121 (10.7)	9/117 (7.7)	1.40 (0.62–3.14)	0.50
Vascular complications				
Major	14/121 (11.6)	14/117 (12.0)	0.97 (0.48–1.94)	1.00
Minor	5/121 (4.1)	2/117 (1.7)	2.42 (0.48–12.22)	0.45
Endocarditis	2/116 (1.7)	1/111 (0.9)	1.91 (0.18–20.81)	1.00
Valve thrombosis	4/116 (3.4)	0/111 (0.0)	–	0.12
Repeat procedure for valve-related dysfunction	2/121 (1.6)	3/117 (2.6)	0.64 (0.11–3.79)	0.68
New pacemaker	26/111 (23.4)	38/100 (38.0)	0.62 (0.41–0.94)	0.02
New-onset atrial fibrillation	8/82 (9.8)	8/85 (9.4)	1.04 (0.41–2.63)	1.00
Combined efficacy endpoint	24/116 (20.7)	31/111 (27.9)	0.74 (0.47–1.18)	0.22
MACCE	13/121 (10.7)	8/117 (6.8)	1.57 (0.68–3.65)	0.36
NYHA functional class improvement	82/95 (86.3)	85/95 (89.5)	0.96 (0.87–1.07)	0.66
Quality-of-life score	65 ± 22	67 ± 20	–	0.49

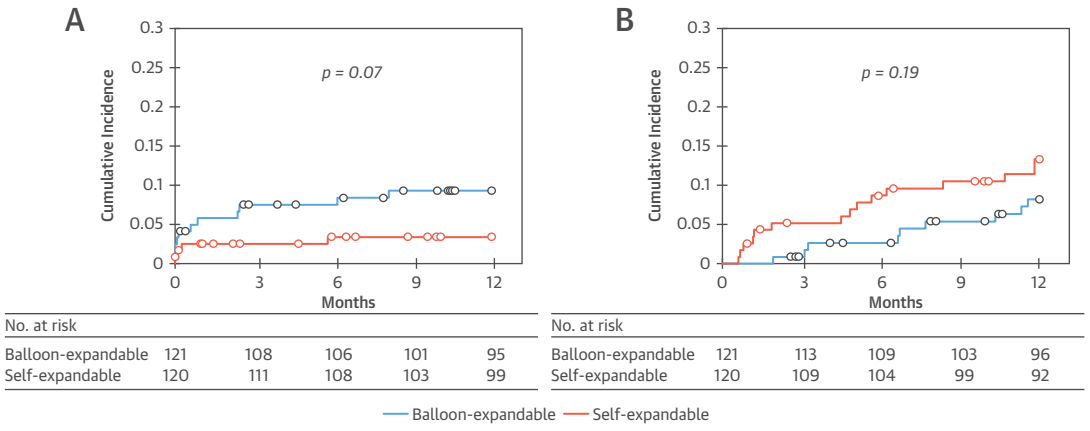
Values are n/N (%) or mean ± SD, unless otherwise noted. The p values for event rates were calculated using Fisher exact tests.
CI = confidence interval; MACCE = major adverse cardiovascular and cerebrovascular event(s); NYHA = New York Heart Association; RR = relative risk.

FIGURE 2 Time-to-Event Curves for All-Cause and Cardiovascular Mortality



(A) Cumulative incidence curves for all-cause mortality by device type. **(B)** Cumulative incidence curves for cardiovascular mortality by device type. Events were calculated using Kaplan-Meier methods, and the p values were calculated using log-rank tests.

FIGURE 3 Time-to-Event Curves for All Strokes and Rehospitalization for Heart Failure



(A) Cumulative incidence curves for stroke by device type. **(B)** Cumulative incidence curves for rehospitalization for heart failure by device type. Events were calculated using Kaplan-Meier methods, and the p values were calculated using log-rank tests.

year, the majority of patients in both groups were in NYHA functional class I or II (88.9% in the balloon-expandable group and 93.9% in the self-expandable group), and NYHA functional class improvement between baseline and 1 year was not statistically significantly different between the groups (86.3% vs. 89.5%; p = 0.66). Quality-of-life score (on a scale ranging from 0 to 100) at 1 year was similar in both groups (mean 65 ± 22 vs. 67 ± 20; p = 0.49).

Results of a landmark analysis for selected clinical endpoints occurring between 30 days and 1 year are shown in **Table 3**. All results were essentially unchanged when sex was taken into account.

ECHOCARDIOGRAPHIC FINDINGS. Echocardiographic follow-up at 1 year was performed in 89.6% of survivors (89.0% of the balloon-expandable group and 90.2% of the self-expandable group) (**Table 4**). Similar to the post-procedural and 30-day findings (12), more than mild paravalvular and total AR were less common in the balloon-expandable group (1.1% vs. 12.1%, p = 0.005, for paravalvular AR; 1.1% vs. 13.1%, p = 0.02, for total AR). Among 177 patients with paired echocardiographic evaluations at hospital discharge and 1 year, paravalvular AR remained unchanged in 59.4% of patients, was improved in 20.3%, and was worse in 20.3%, with no differences in the evolution of AR over time between balloon- and self-expandable valves (p = 0.98) (**Table 5**, Online Tables 1 and 2).

In contrast, the median transvalvular gradient remained slightly but statistically significantly higher in the balloon-expandable group at 1 year (median 9 mm Hg [IQR: 7 to 12 mm Hg] vs. 8 mm Hg [IQR: 5 to 11 mm Hg]; p = 0.004). Four patients of the balloon-expandable group had elevations of mean transvalvular gradient and reductions of aortic valve area recorded during the follow-up period, which were not recorded post-procedurally (observed between 175 and 203 days after TAVR; the mean gradient was higher than 30 mm Hg in all 4 patients). A mobile

TABLE 3 Landmark Analysis of Key Clinical Outcomes Between 30 Days and 1 Year

	Balloon-Expandable Valve	Self-Expandable Valve	RR (95% CI)	p Value
Death of any cause	16/116 (13.8)	9/111 (8.1)	1.70 (0.78-3.69)	0.21
Stroke	4/111 (3.6)	1/109 (0.9)	3.93 (0.45-34.59)	0.37
Ischemic stroke	3/111 (2.7)	1/109 (0.9)	2.95 (0.31-27.89)	0.62
Hemorrhagic stroke	1/111 (0.9)	0/109 (0.0)	–	1.00
Repeat hospitalization for heart failure	9/116 (7.8)	13/110 (11.8)	0.66 (0.29-1.47)	0.37
New pacemaker	7/89 (7.9)	0/58 (0.0)	–	0.04

Values are n/N (%). For mortality, patients who died during the first 30 days were excluded. For all other endpoints, patients who either died or had events in the first 30 days were excluded. The p values were obtained using Fisher exact tests.

Abbreviations as in **Table 2**.

mass suspicious for thrombus was detected in 1 patient, and leaflet thickening and restricted motion were observed in the remaining 3 patients. All 4 patients had completed at least 3 months of dual-antiplatelet therapy (3 were on aspirin monotherapy and 1 on dual-antiplatelet therapy at the time of diagnosis). In all 4 patients, the transvalvular gradient normalized with anticoagulant therapy, suggesting a thrombotic etiology.

Consequently, prosthetic valve dysfunction as defined by the VARC was recorded in 2.6% of patients in the balloon-expandable group and 11.7% of patients in the self-expandable group at 1 year ($p = 0.009$). The VARC-defined combined efficacy endpoint at 1 year was not statistically significantly different between the groups (20.7% vs. 27.9%, respectively; $p = 0.22$).

DISCUSSION

The main findings of this 1-year analysis of the randomized CHOICE trial are as follows: 1) paravalvular regurgitation remained stable, without significant worsening or improvement during follow-up, with both balloon- and self-expandable devices, and more than mild forms remained lower with the balloon-expandable valve; 2) probable valve thrombosis was infrequent but was observed only in patients receiving the balloon-expandable valve; and 3) mortality was not statistically significantly different at 1 year, but clinical events with a strong impact on mortality tended to be different between both devices (numerically lower repeat hospitalizations for heart failure but higher stroke rates with the balloon-expandable valve).

PARAVALVULAR LEAKS. The primary endpoint of the CHOICE trial (device success) was driven largely by differences in post-procedural AR rates favoring the balloon-expandable valve (12). These differences were observed using various methods of AR assessment, including angiography (core laboratory graded), echocardiography (site graded), and quantitative cardiac magnetic resonance imaging shortly after the procedure. Findings from the randomized PARTNER (Placement of Aortic Transcatheter Valves) trial have shown that paravalvular AR after the implantation of a balloon-expandable valve remained stable during follow-up (18). However, the majority of patients with moderate or severe paravalvular AR shortly after the implantation of a self-expandable device in the randomized U.S. CoreValve trial had only mild or no regurgitation at 1 year (3,4). This potential improvement over time was attributed to the use of computed tomographic assessment of aortic annular diameter for valve-size selection, higher placement of the valve within the aortic annulus, and sustained expansion of the nitinol frame of the self-expanding device (3). Despite the use of computed tomographic assessment in the vast majority of the CHOICE population and the high placement of the

TABLE 4 Echocardiographic Follow-Up at 1 Year

	Balloon-Expandable Valve	Self-Expandable Valve	p Value
Number of patients	69	66	
Effective orifice area, cm^2	1.7 ± 0.4	1.8 ± 0.6	0.34
Number of patients	68	66	
Indexed effective orifice area, cm^2/m^2	0.9 ± 0.2	1.0 ± 0.3	0.16
Number of patients	79	81	
Mean gradient, mm Hg	9 (7–12)	8 (5–11)	0.004
Number of patients	88	91	
Transvalvular aortic regurgitation			0.44
None/trace	86 (97.7)	86 (94.5)	
Mild	2 (2.3)	5 (5.5)	
Moderate	0 (0)	0 (0)	
Severe	0 (0)	0 (0)	
Number of patients	89	91	
Paravalvular aortic regurgitation			0.01
None/trace	52 (58.4)	44 (45.6)	
Mild	36 (40.4)	36 (39.6)	
Moderate	1 (1.1)	11 (12.1)	
Severe	0 (0)	0 (0)	
Number of patients	89	92	
Total aortic regurgitation			0.03
None/trace	51 (57.3)	42 (45.6)	
Mild	37 (41.6)	38 (41.3)	
Moderate	1 (1.1)	11 (12.0)	
Severe	0 (0)	1 (1.1)	
Left ventricular ejection fraction, %	58.9 ± 10.9	57.3 ± 11.8	0.37
Left ventricular end-systolic dimension, mm	32.6 ± 8.8	34.6 ± 8.1	0.10
Left ventricular end-diastolic dimension, mm	46.1 ± 8.1	48.2 ± 7.4	0.16
Systolic pulmonary artery pressure, mm Hg	28.4 ± 10.5	32.3 ± 13.0	0.06
Moderate/severe mitral regurgitation	13/88 (14.8)	28/90 (31.1)	0.01
Moderate/severe tricuspid regurgitation	12/85 (14.1)	20/88 (22.7)	0.14

Values are n, mean ± SD, median (interquartile range), or n/N (%).

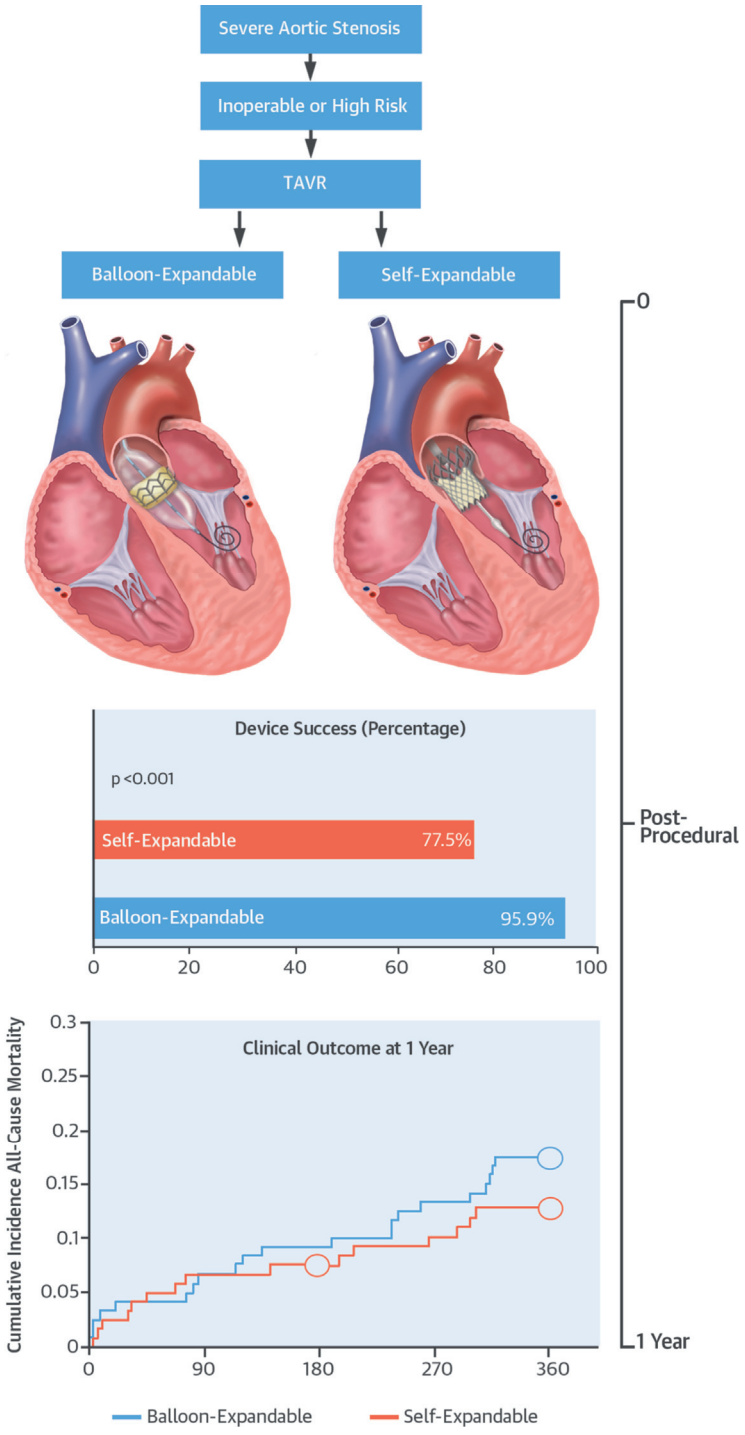
TABLE 5 Changes in PVL for Balloon- and Self-Expandable Valves: Echocardiography at Discharge Compared With 1 Year (Patients With Data at Both Time Points)

Change in PVL Grade Between Discharge and 1 Year	Balloon-Expandable Valve	Self-Expandable Valve	p Value*
−2	0/88 (0)	1/89 (1.1)	0.98
−1	15/88 (17.0)	20/89 (22.5)	
0	58/88 (65.9)	47/89 (52.8)	
1	15/88 (17.0)	21/89 (23.6)	

Values are n/N (%). *The p value for comparison between balloon- and self-expandable valves obtained with the Mann-Whitney *U* test.

PVL = paravalvular leak.

CENTRAL ILLUSTRATION **1-Year Outcomes After Transcatheter Aortic Valve Replacement With Balloon-Expandable Versus Self-Expandable Valves**



Abdel-Wahab, M. et al. J Am Coll Cardiol. 2015; 66(7):791–800.

The design of CHOICE (Randomized Comparison of Transcatheter Heart Valves in High Risk Patients With Severe Aortic Stenosis: Medtronic CoreValve Versus Edwards SAPIEN XT) is illustrated, showing the results of its previously reported primary endpoint and the main secondary endpoint at 1 year. TAVR = transcatheter aortic valve replacement.

valve within the aortic annulus (5 mm below the annular plane), we did not observe a reduction of overall AR rates with the self-expanding valve over time. In the self-expanding group of the CHOICE trial, 5 of 7 patients (71%) with moderate AR at discharge had mild or no AR at 1 year, but 9 of 45 patients (20%) with mild AR at discharge progressed to moderate AR, resulting in a neutral effect on the overall incidence of different AR grades observed during follow-up echocardiography.

VALVE THROMBOSIS. An unexpected finding during the 1-year follow-up period was the occurrence of early prosthetic valve dysfunction possibly attributed to valve thrombosis in 4 patients treated with balloon-expandable valves (incidence of 3.4%). Thrombosis of transcatheter valves was first described by Latib et al. (19) in a series of 3 patients treated with the balloon-expandable Edwards SAPIEN XT valve. In a recently published systematic review of published cases, Córdoba-Soriano et al. (20) reviewed a total of 11 publications describing 16 patients thought to have developed valve thrombosis after TAVR. All but 1 patient (94%) received balloon-expandable valves, and all patients received dual-antiplatelet therapy immediately after the procedure and continued to receive either single- or dual-antiplatelet therapy at the time of valve thrombosis diagnosis. Valve thrombosis was diagnosed at a median of 6 months post-procedurally (similar to our findings), and significant increases in transvalvular gradient and leaflet thickening were the most common echocardiographic features. In the majority of patients, valve function was effectively restored with anticoagulant therapy. Although it remains difficult to determine the exact mechanisms for these observations, it is likely that thrombosis after TAVR relates to an interplay of various anatomic, procedural, and valve-related factors (20). Differences in how the prosthesis is deployed (balloon inflation vs. self-expansion) and its adaptation on the ovular native aortic annulus might provide different interactions with the surrounding anatomic structures, potentially promoting thrombosis (20,21). Importantly, no differences in adjunctive antiplatelet or anticoagulant therapy were observed in the CHOICE trial between the treatment arms (Online Table 3).

CLINICAL OUTCOMES. Symptomatic improvement in the CHOICE trial was maintained at 1 year, with no statistically significant differences between the devices. Clinical endpoints, particularly all-cause and cardiovascular mortality, were not statistically significantly different between the devices and were comparable with contemporary outcome data with both device types in Europe and the United States (3–5,9,10,22). This is in line with previously published registry data comparing balloon- and self-expandable TAVR devices, which failed to show any difference in survival at short- and intermediate-term follow-up between the valves (7,9–11). Despite the differences in relevant outcome measures such as paravalvular AR and device success favoring the balloon-expandable valve, and the association of device success with improved survival in this trial (data not shown), mortality rates were not statistically significantly different at 1 year (**Central Illustration**). This could be partially explained by the moderate sample size of this study, which was not powered to detect differences in clinical outcomes, and the ongoing "background" events of death that occur in patients in their 80s. However, a relevant clinical event associated with mortality, such as stroke, tended to be less common with the self-expandable device, which may have counterbalanced the advantage of a higher device success rate in the balloon-expandable group. A potential relationship between stroke and valve thrombosis in the balloon-expandable group remains speculative, as none of the patients with probable valve thrombosis in this trial had thromboembolic complications. In a recently published meta-analysis, stroke rates were comparable between balloon- and self-expandable valves at 30 days (3.0% vs. 2.4%, respectively) (23). The rates of cerebrovascular events at 1 year in the high-risk cohorts of the randomized PARTNER and U.S. CoreValve trials were 8.3% and 8.8%, respectively (2,3).

STUDY LIMITATIONS. The 1-year findings of this trial should be interpreted in the context of its moderate sample size and the lack of power to detect differences in clinical outcomes. As previously described (12), the lack of an echocardiographic core laboratory remains a limitation of this trial. However, the echocardiographic evaluation of the severity of paravalvular leaks after TAVR remains complex and challenging, and differences in grading have even been observed within and between different echocardiographic core laboratories (24).

CONCLUSIONS

Despite the higher device success rate and lower paravalvular regurgitation rate (which remained stable during follow-up) with the balloon-expandable valve, no statistically significant differences in 1-year mortality rates were observed among the CHOICE patients treated with either balloon- or self-expandable valves, with limited statistical power. The numerically higher rate of thromboembolic

events with the balloon-expandable valve underscores the necessity of adequately powered large comparative device trials in the TAVR field.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: In patients undergoing TAVR because they would have faced a high risk for complications with surgical aortic valve replacement, there was no statistically significant difference in 1-year survival between balloon-expandable and self-expandable devices.

TRANSLATIONAL OUTLOOK: Additional studies are needed to compare the safety and efficacy of available devices during long-term follow-up of patients with aortic valve disease undergoing TAVR.

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KEY WORDS aortic stenosis, balloon-expandable, self-expandable, TAVR

APPENDIX For a list of the CHOICE trial participants and supplemental tables, please see the online version of this article.